IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

In Re Application of: James P. Elia	)	Docket No.: 1000-10-CO1
Serial No.: 09/836,750	)	Group Art Unit: 1646
Filed: April 17, 2001	)	Examiner: Elizabeth C. Kemmerer, Ph.D.
For: METHOD FOR GROWING MUSCLE IN A HUMAN HEART	)	

MAIL STOP APPEAL BRIEF
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APPELLANT'S APPEAL BRIEF

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I hereby certify that the attached APPELLANT'S APPEAL BRIEF was deposited, as First Class Mail, in an envelope addressed to: Mail Stop APPEAL BRIEF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 this 20th day of February, 2007.

Dated: 2/20/07

Gerald K. White

Printed Name: GERALD K. WHITE

GERALD K. WHITE & ASSOCIATES, P.C.
205 W. Randolph Street
Suite 835
Chicago, IL 60606
Phone: (312) 920-0588
Fax: (312) 920-0580
Email: gkwpatlaw@aol.com

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REAL PARTY IN INTEREST

The real parties in interest in the instant appeal are Assignees, Dental Marketing Specialists, Inc., an Arizona corporation, 9377 E. Bell Road, Suite 385 Scottsdale, Arizona 85260, and Jerry W. Bains and Salee C. Bains Irrevocable Trust, 9013 Red Lawrence Drive, Carefree, Arizona 85377. Subsequent to the assignment recordal for the instant application, the address of Dental Marketing Specialists, Inc., changed to 7364 East Crimson Sky Trail, Scottsdale, Arizona 85262. Also, subsequent to the assignment recordal for the instant application, the address of Jerry W. Bains and Salee C. Bains Irrevocable Trust, changed to 39096 N. 102nd Way, Scottsdale, Arizona 85262.

RELATED PROCEEDINGS

There is one appeal proceeding known to Appellant's legal representatives, which may be related to, directly affect, or may have a bearing upon the Board's decision in the pending appeal. Such appeal proceeding is that taken for co-pending Serial No. 09/794,456, filed February 27, 2001, in which Appellant's Brief was filed with the Patent and Trademark Office on February 8, 2007. There are no related interferences or judicial proceedings known to Appellant, Appellants' legal representatives, or Assignee, which may be related to, directly affect, be directly affected by, or may have a bearing on the Board's decision in the pending appeal. The attached Related Proceedings Appendix confirms the above statements.

STATUS OF CLAIMS AND CLAIMS UNDER APPEAL

Claims 1-5 were cancelled in the Preliminary Amendment filed April 17, 2001.

Claims 204, 205, and 237 were cancelled in the Amendment filed February 17, 2004.

Claims 254-256 were cancelled in the Amendment filed November 21, 2005.

Claims 6-235 and 240-242 stand withdrawn, by the Examiner, from consideration as being directed to a non-elected invention. Claims 204 and 205 were cancelled by Appellant and thus were incorrectly identified by the Examiner as being withdrawn.

Claims 245, 248, 249, 252, 264-267, and 272-279 are hereby withdrawn by Appellant from the instant appeal. Such or similar claims are pending in continuation application Serial No. 11/605,153, filed November 28, 2006. By filing such continuation application, Appellant has chosen to reduce the number of issues for the instant appeal and does not acquiesce to, or in any way agree with, the correctness of any rejection of these claims in the prosecution of the present application.

Claims 286 and 287 are hereby withdrawn by Appellant from the instant appeal. Such or similar claims are pending in application Serial No. 09/794,456, filed February 27, 2001. Appellant is satisfied to pursue such claims in said application instead of the instant application thereby reducing the number of issues in the instant appeal.

In view of the above-identified withdrawal of claims, the correctness of the Examiner's Final Rejection of claims 236, 238, 239, 243, 244, 246, 247, 250, 251, 253, 257-263, 268-271, and 280-285 under 35 U.S.C. §112, first paragraph, for lack of enablement constitutes the sole issue on appeal.

Appellant notes that appealed claim 246 depends upon withdrawn claim 245, which in turn depends upon appealed claim 244. Rather than file an Amendment requiring that claim 246 depend upon claim 244, Appellant respectfully requests the Board, for purposes of the instant appeal, to consider claim 246 as having such dependency. Appellant proposes to amend claim 246 to depend upon claim 244 at an appropriate time.

STATUS OF AMENDMENTS

No amendment has been made or entered subsequent to the Final Rejection of September 22, 2006.

SUMMARY OF CLAIMED SUBJECT MATTER

Appellant's invention is directed to a method of using well-known compositions (materials), old and well-known administration techniques for such compositions, and equally old and well-known medical apparatus to produce a novel result, i.e., the use of growth factors, including a cell (stem cell), such as bone marrow stem cells ("BMC's"), to grow a new artery and new cardiac muscle in the heart of a human patient and also to growing such new artery and cardiac muscle and repair a dead or damaged portion of a heart. Antecedent bases in the specification for various claim elements are included below.

Appellant's novel contribution to the medical art is defined in the broadest scope in generic claim 236 on appeal as comprising a method for growing a new portion of a human heart by placing a growth factor in the body of a human patient and forming a new artery and new cardiac muscle thereby and claims 238 and 239 cause repair of dead and damaged portions of the heart with the growth of new arteries and cardiac muscle (page 45, lines 17-22; page 46, lines 3-14). A growth factor, as called for by claim 236, broadly encompasses compositions and living organisms, which promote the growth of soft tissue in the body of a patient (page 20, lines 10-14). Appellant's specification on page 21 broadly recites that, "The growth factor can be administered orally, systemically, in a carrier, by hypodermic needle...or by any other desired method." Appellant's invention specifically describes using patient size, vascularity, simplicity of access, ease of exploitation, or any other desired factors in determining the selected area of the patient for administrating said growth factor (page 45, lines 1-16). Appellant describes dosages

of growth factors useful for achieving growth of a new artery and achieving heart repair as defined in claims 236, 238, and 239 (page 53, lines 13-19; page 56, lines 7-19; and page 62, lines 1-10) and describes monitoring heart repair by determining blood flow through the new artery by using any readily available commercial device such as ultrasound, angiogram, etc. (page 56, lines 20-25). The specification on page 47 discloses that booster shots of growth factor may be required to repair an organ that is not operating at a desired capacity.

Appellant's elected invention is defined in claim 243, which directly depends from claims 236, and specifically limit the growth factor to a subgenus comprising a member selected from the group consisting of cells, cellular products, and derivatives of cellular products and claim 246 which limits the growth factor to stem cells (page 37, lines 19-26). Claims 244 and 271 further limit the invention by specifying that the growth factor of claims 243 and 259, respectively, comprises a cell (page 37, lines 19-26). Claims 247, 268, and 269 directly depend from claims 236, 262, 263, respectively and further limit the method of said claims 236, 262, and 263, respectively, by reciting that the growth factor is placed in said patient by injection (page 21, line 5; page 45, line 14); and claim 251 depends from and further limits the method of claim 236 by requiring the growth factor be placed in said patient by a carrier (page 21, lines 3-6). Claim 253 depends from claim 236 and requires that the growth factor comprises a gene and a cell (page 46, lines 6-9). Claims 257, 258, 259, and 260 directly depend from and further limit claims 236, 238, 239, and 243, respectively, by requiring that the growth factor is locally placed in the human body (page 21, lines 4-10 and page 46, lines 3-9). Claims 261, 262, and 263 directly depend from and further limit claim 236, 238, and 239,

respectively, by requiring that the growth factor involved in the growth of new arteries and new cardiac muscle (claim 261), the repair of dead portions of the heart (claim 262), and the repair of damaged portions of the heart (claim 263) comprises living stem cells harvested from bone marrow (page 40 lines 27 – page 42, line 30). Claims 270 and 271 directly depend from claims 258 and 259, respectively and require placing a cell into the heart adjacent a dead (claim 270) or damaged (claim 271) portion of the heart causing new arteries and new cardiac muscle to be grown and repair of dead (claim 270) and damaged (claim 271) portions of a human heart to be repaired (pages 45 and 46). Claims 280, 281, and 282 directly depend from claims 236, 238, and 239, respectively and require calculating blood flow through the newly grown artery (page 56, lines 20-25). Such calculation provides an indication of artery growth. Claims 283, 284, and 285 directly depend from claims 236, 238, and 239, respectively, and require observing the newly grown arteries (page 56, lines 20-25). Such observation provides a description of artery growth.

GROUNDS OF REJECTION FOR REVIEW ON APPEAL

Appealed claims 236, 238, 239, 243, 244, 246, 247, 250, 251, 253, 257-263, 268-271, and 280-285 stand finally rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

ARGUMENT

Rejection of Claims 236, 238, 239, 243, 244, 246, 247, 250, 251, 253, 257-263, 268-271, and 280-285 Under 35 U.S.C. §112, first paragraph

As a preliminary matter, Appellant notes that the withdrawal of the above-mentioned claims from the instant appeal renders moot the Final Rejection of claims 248, 249, 252, and 274-279 under 35 U.S.C. §112, first paragraph, new matter; the Final Rejection of claim 245 under 35 U.S.C. §112, second paragraph, indefinite; and the Final Rejection claims 286 and 287 for double patenting.

The Examiner finally rejected appealed claims 236, 238, 239, 243, 244, 246, 247, 250, 251, 253, 257-263, 268-271, and 280-285, "under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement." Specifically, the Examiner, on pages 7 and 8 of the Final Rejection dated September 22, 2006, states that:

> The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Appellant disagrees that the scope of protection provided by the appealed claims is not adequately enabled by the application disclosure. Appellant intends to, and does hereinafter, argue the patentability of each claim separately, i.e., the patentability of the claims on appeal do not stand or fall together.

At the outset, Appellant believes that there are three important factors to consider when determining whether the instant specification contains a disclosure that would have enabled a skilled person in the medical art to make and use the claimed invention. When these factors are considered, there can be no doubt that Appellant's specification provides an enabling disclosure. The three factors are discussed below.

First, as pointed out in the Summary of Claimed Subject Matter portion of the instant Brief, there is a considerable body of disclosure relating to Appellant's generic invention of repairing organs in human patients, including the heart, by forming a new cardiac muscle and artery and of elected and non-elected growth factors suitable for effecting such repair and formation. In this regard, Appellant's specification provides a substantial body of disclosure regarding growing and/or replacing organs and/or forming arteries and tissues using well-known growth factors. The specification describes a class of growth factors that broadly and specifically includes genes, nucleic acids, a patient's own cells, or universal cells, e.g., stem cells, etc., all of which are described to promote tissue growth through differentiation and morphogenesis. The Examiner has only considered the disclosure regarding enablement as it specifically relates to the elected growth factor species, cells. The Examiner's selective reading, which ignores Appellant's broad and specific disclosure relating to non-elected growth factor species disclosure, is clearly erroneous under relevant case law. When an applicant elects to prosecute a species following an election requirement, the Examiner is not permitted to wear blinders and focus solely upon the elected species and ignore the scope of enablement provided by the specification as a whole. There should be no doubt that the specification taken as a whole, when properly read and understood by one skilled in the art, meets the statutory requirement for enablement under current law.

It is clear that the Examiner intended to so erroneously limit her review of the application disclosure from the statement at page 6, lines 1-8 of the February 22, 2006,

Office Action in co-pending patent application Serial No. 09/794,456, filed February 27, 2001 that:

> The claims are being examined to the extent that they read on the elected invention, administration of cells, and thus the generic concept of growth factor is not relevant. (emphasis added)

It is evident that the Examiner also erroneously ignored disclosure related to non-elected species, such as genes and proteins, in evaluating enablement. In this regard, for example, please see page 10, lines 4-7 and page 12, lines 14-21 of the Final Rejection of September 22, 2006.

Second, the Examiner has not taken issue with the fact that the administration techniques and administered materials disclosed by Appellant were individually old and well known as of the filing date of the instant patent application. The materials and administration techniques disclosed by Appellant were routinely employed in the medical art, but not in the claimed combination, at the time the instant application was filed. Appellant's contribution to the medical arts resides in the claimed method of treating a heart in a human patient by implanting cells in said patient and growing cardiac muscle and an artery in said heart.

Third, the Examiner stated that the level of skill in the art is high. Appellant agrees that the skill level is high when it is considered that many years of education, training, and experience are required in the medical field.

Once the above-identified relevant materials and administration techniques set forth in Appellant's specification are properly considered in their entirety, Appellant believes that there should be no question that one skilled in the medical art is enabled to make and use the claimed invention. This conclusion is reinforced, as noted above, by

the fact that the materials and administration techniques, but not the inventive results, were well known when the instant application was filed. MPEP Section 2164 states that the purpose of the enablement requirement is to describe the claimed invention in such terms to permit one skilled in the art to make and use the invention. Such Section cautions that detailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention. MPEP Section 2164.01 states that:

> A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F2d. 660, 661, 18 USPQ 2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F2d. 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986) cert denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 730 F2d. 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Appellant believes that the above caution is especially relevant to the instant factual situation where the Examiner has conceded that there was a high level of skill in the art at the time the instant application was filed, coupled with the fact that the Examiner has not taken issue with Appellant's position that all the materials, methods, and apparatus needed to practice the invention were well known at the time of the invention. Thus, Appellant submits that the instant disclosure clearly enables one skilled in the medical arts to make and/or use the full scope of the claimed invention without undue experimentation because a reasonable consideration of the three above-delineated factors and the interaction thereof leads to the inevitable conclusion that the disclosure is enabling.

The Examiner has the burden to establish and support by convincing objective evidence a *prima facie* case of lack of enablement. For reasons set forth below, Appellant believes the Examiner has failed to meet such burden.

The Board's attention is respectfully directed to page 11 of the Final Rejection, where the Examiner concluded:

> Due to the large quantity of experimentation necessary to determine how to effectively administer cells to achieve *de novo* formation of cardiac muscle and an artery and thereby grow a new portion of a pre-existing heart, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the contradictory state of the prior art, the unpredictability of the effects of an agent on a physiological response, and the breadth of the claims which fail to recite limitations regarding cell type or dosage or site of delivery, etc., undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope (emphasis added).

As plainly evident, the Examiner's conclusion is of a conditional nature, i.e., the rejection depends upon the achievement of *de novo* cardiac muscle and arteries. However, neither the specification nor the claims are directed to *de novo* cardiac muscle and arteries. The condition established by the Examiner to measure enablement of the claims, i.e., the achievement of *de novo* cardiac muscle and arteries, is not present in the claims; and the rejection must be reversed as not being relevant to the claimed invention.

Appellant submits that the construction of the appealed claims accorded by the Examiner on pages 8 and 11 of the Final Rejection of September 22, 2006 as requiring *de novo* cardiac muscle and artery formation is clearly erroneous. The Examiner's statement that, "Applicant has defined a new artery as an organ comprising two or more kinds of tissue..." is incorrect and misleading (emphasis added). The specification on page 44

defines the term "organ" used by Appellant as consisting "of two or more kinds of tissues joined into one structure that has a certain task." The Examiner's statement that, "Applicant appears to imply that the 'new artery' recited in the claims must be formed de novo, and not merely repair, growth or re-direction of an existing artery," is also incorrect and misleading. Appellant made no such statement or implication. Appellant's specification at pages 45-50 describes that growth factors are utilized to "grow" and for "forming" new muscles and arteries and to facilitate differentiation into organs or function specific tissues, including muscle tissue and arteries. The specification at pages 54, 56, and 62 clearly defines the claimed term "new artery," and the scope of the claims is legally determined by this disclosure. It is clear from such disclosure what Applellant intended the term "new artery" to mean. See Philips v. AWH., Corp., 03-1269-1286, decided July 12, 2005.

The Examiner, not Appellant, appears to have coined the term "*de novo* artery" and thus becomes its lexicographer. The Examiner has not explained what is encompassed by such term nor has she provided any evidence in this record which defines or recognizes the scientific relevance of such term. Further, the Examiner has failed to point to any language in the claims or description in the subject application limiting Appellant's claimed invention to the formation of *de novo* arteries. The Examiner's attempt to support her position by stating at page 8 of the Final Rejection, "See the discussion regarding fusion versus formation of new cells," (referring to Appellant's February 17, 2004 Amendment) does not clearly identify any alleged implication of Appellant that a new artery must be formed *de novo*. Appellant has reviewed the February 17, 2004 Amendment and finds that it used the term "fusion" at

pages 42 and 45. Such usage is unrelated to the term *de novo* arteries, and thus Appellant is at a loss as to how to respond to the Examiner's statement. Appellant stands ready to respond, via a Reply Brief, to any other portion once it is identified by the Examiner. The Examiner has taken Appellant's remarks in the above-mentioned Amendment out of context. Appellant's remarks in that response were directed to distinguishing the present invention from the Murry et al. (hereinafter "Murry" and of record) reference's implantation of skeletal satellite (stem) cells in murine models, which did not result in artery growth. Appellant did not explicitly or implicitly argue that the present invention distinguishes over Murry by *de novo* growth of arteries.

Accordingly, the Examiner's enablement determination is conditional to the extent it is bottomed on the specification's failure to provide enablement for the achievement of *de novo* arteries. The Examiner's conditional rejection is patently erroneous and, perforce, should be summarily reversed.

Even though Appellant believes that the Examiner committed reversible error in misconstruing the scope of the claims and conditionally rejecting the claimed subject matter based on such construction, a full treatment of the Final Rejection as best understood follows.

The first paragraph of the statue requires nothing more than objective enablement, and it is of no importance whether such teaching is set forth by use of illustrative examples or by broad terminology. As a general matter, an application disclosure, which contains a teaching of how to make and use the invention in terms which correspond in scope to those used in describing the invention sought to be patented, is considered to be in compliance with the enabling requirement of the statue. In re Marzocchi, 58 CCPA

1069, 439 F.2d 220, 169 USPQ 367, 369-370 (1971). Further, "Section 112 does not require that a specification convince persons skilled in the art that the assertions therein are correct." [Emphasis added]. In re Robins, 429 F.2d 452, 166 USPQ 552 (CCPA, 1970).

When evaluating enablement, it is incumbent upon the Examiner to determine what subject matter each claim recites, i.e., the scope of protection sought for each claim. The scope of dependent claims are properly determined with respect to 35 U.S.C. §112, fourth paragraph. See MPEP Section 2164.08. It is clear that the Examiner's analysis did not treat the subject matter of each claim separately or treat the dependent claims according to statutory mandate. The only claims that the Examiner addressed regarding the specifically claimed subject matter in the Final Rejection were withdrawn claims 248, 249, and 274-277, which specifically recite intraveneous, intraluminal, and angioplasty modes of delivery. The appealed claims do not specifically require such withdrawn subject matter. The Examiner states that the underlying fact at issue is whether or not more than routine experimentation would be required to practice the claimed invention and addresses this issue by reference to the guidelines established in In re Wands, 858 F.2d 731, 737, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). As evidence in support of her non-enablement determination, the Examiner relies on the Strauer et al. (hereinafter "Strauer"), Deb et al. (hereinafter "Deb"), and Murry publications (all of record). None of these publications specifically teaches intramuscular injection of stem cells into a human patient's heart and growing an artery as required by claims 272 and 273 and thus are not relevant to the enablement of such claims.

Initially, Appellant points out that it is evident the Examiner failed to consider the disclosure provided by Appellant's specification as a whole in determining compliance with the enablement requirement of the statute. The appropriate factual determination is whether the instant specification reasonably teaches one skilled in the art how to make and use the claimed subject matter. As demonstrated above, the Examiner erroneously restricted the factual determination to the elected species of growth factor and, thusly, ignored those portions of the specification describing a broader generic invention and also ignored disclosure related to non-elected species. Appellant is entitled to have the entire disclosure considered in determining compliance with 35 U.S.C. §112, first paragraph. See In re Anderson, 471 F2d. 1237, 176 USPQ 331, (CCPA 1973) and In re Johnson and Farnham, 558 F.2d 1008, 194 USPQ 187, 195 (CCPA 1977). Further, it is well settled that the test for enablement must take into consideration that which is known in the prior art – that a patent should preferably omit that which is well known/understood in the particular art to which the claims are directed. See MPEP Section 2164.01 and the authorities cited therein.

Appellant submits that a careful analysis of the Wands factors in light of the application disclosure compels a conclusion that undue experimentation would not be required to practice the claimed invention. Contrary to the Examiner's assertion, the Strauer publication does not disclose any experimental protocol required for practicing the invention. Rather, Strauer discloses following protocols that were routinely used in the art and employing an off-the-shelf angioplasty balloon catheter, such as, for example, a catheter of the type described in Nabel et al, U.S. Patent No. 5,328,470 (of record), for transplanting autologous bone marrow mononuclear cells to treat acute myocardial

infarction (MI) in human patients. The concept of containment to prevent backflow and prolong contact time is clearly taught by Nabel et al. Thus, contrary to the Examiner's assertions, it is clear that Strauer did not have to perform any experimentation in order to choose an appropriate delivery system or devise a containment system that would prevent backflow of cells and thus provide a prolonged time for cell implantation. Appellant's specification provides direction and guidance in regard to the well known use in the prior art of a containment system for controlling "carry away" and prolonged contact of cells in Examples 18 and 19 in regard to injection of cells. It is important to note that claims 247, 250, 268, and 269 specifically recite injecting cells, and the Examiner has not critically reviewed the enablement provided by Appellant's disclosure *vis-à-vis* the scope of these claims. The Examiner has conceded, at page 22 of the Final Rejection, that the administration of cells is old in the art. Strauer does not describe using any experimental protocol to determine appropriate cell population, i.e., there is no requirement for experimentation described by Strauer for determining or using specific bone marrow stem cell species. Regarding time of treatment, Strauer does not disclose that determining time of treatment required experimentation. Strauer (published in 2002) elected to treat patients following five to nine days after suffering an MI. Note that a later publication of Strauer, the 2005 Strauer publication (of record), discloses treating chronic MI in patients that had transmural MI some 27 months earlier. Again, no experimentation regarding treatment time was noted. It is evident that the time of treatment following an MI is not a critical variable and undue experimentation would not be required. To the extent that the Examiner may be relying on Murry's murine models to establish that the time of administration is critical, Appellant points out that Strauer

2005 is the "best evidence" in regard to whether time of treatment in human patients is critical. Strauer 2005 teaches that stem cells can be used to successfully treat MI in human patients suffering either acute or chronic disease. Thus, the Examiner's conclusion that "great quantities of experimentation" would be required to practice the claimed invention is not supported on the record and is fatally flawed.

The Examiner's contention that, "The specification provides no guidance along the lines of the details worked out by Strauer," is misplaced. Firstly, none of the claims on appeal require the use of an angioplasty balloon catheter; and, therefore, it is improper for the Examiner to look solely to Strauer for guidance. Secondly, application Example 19 (page 56) describes a detailed regimen for treating a patient with a damaged heart by injecting a growth factor for promoting artery growth, which includes mode, dosage, and means for evaluating success of treatment. Specifically, Example 19 describes a regimen wherein cells are injected slowly over "a five second time period." The application disclosure also teaches, on pages 40-42, 47, and 48, utilizing autologous stem cells harvested from bone marrow and blood of the patient (self-cell therapy) or from cell cultures (allogenic) to grow organs, i.e., arteries, by differentiation and morphogenesis (page 48).

The Examiner states at pages 10 and 13 of the Final Rejection, "The specification contains only prophetic Examples," and that, "There are no working examples directed to administering stem cells to dead or damaged portions of a heart," but fails to explain how this supports a holding of non-enablement and, for good reason, since actual working examples are not a requisite for satisfying the enabling requirement of the statute. Actual

working examples are not required if the invention is disclosed in a manner that one skilled in the art would be able to practice it. Section 2164.02 of the MPEP states that:

> Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic." A working example is based on work actually performed. A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved.

The Examiner's contention on page 10 of the Final Rejection that, "...none of the prophetic examples are directed to administration of cells to grow a new artery..." is not supported on the record. One skilled in the art reading the specification at page 46, lines 3-8 would reasonably understand that Appellant disclosed a method comprising seeding, e.g., injecting, appropriate cells (stem cells) or other growth factors to promote growth of cardiac muscle and blood vessels (arteries) in a damaged portion of a human heart. Furthermore, one reasonably skilled in the art would understand from page 47, line 22 through page 48, line 15 that a patient's own (autologous) stem cells can be used to grow function specific tissue, such as muscle and arteries, *in vivo* through differentiation and morphogenesis. Those skilled in the art understand that "morphogenesis" is the formation and differentiation of tissues and organs and that an artery is an organ. See pages 33 and 48 of the specification.

Appellants agree with the Examiner that the medical arts in general are complex. However, while the physiological reactions involved may be complex, the practice of the claimed invention is straightforward. The called-for cells, e.g., stem cells, the methods of administering, and the particular apparatus required for administering the cells are old and well known in the medical arts.

The Examiner's statement at page 10 of the Final Rejection that:

> The state of the prior art does not support the specification's (and claims') assertion that a new artery can be grown. None of the numerous post-filing date publications put on the record by Applicant to support enablement of the claimed invention report the *de novo* growth of an artery as defined by Applicant, including Strauer

evinces a misunderstanding of the manner in which the Court applied "the state of the art" factor in In re Wands. The Court applied this factor in determining whether all the materials and methods needed to practice the Wands invention were known in the art. Appellant relies upon the instant specification and not upon any "post-filing date publications" to support enablement. As discussed above, Appellant's specification does not need to support enablement for *de novo* growth of arteries because the claims in issue do not recite or require such a limitation. Moreover, Applicant never defined a new artery as a *de novo* artery, as erroneously alleged by the Examiner.

The Examiner admits that the level of skill in the art was high at the time the instant application was filed.

The Examiner states that the claimed invention is unpredictable because of its use of physiological agents, citing supporting authority. However, the Examiner does not provide any succinct reasoning or evidence as to why one skilled in the art would doubt that the asserted scope of objective enablement in Appellant's specification is not in fact commensurate with the scope of the claims. The specification provides multiple embodiments using multiple well-known species of growth factors for promoting artery growth employing multiple well-known administration modes carried out with multiple well-known apparatus.

The Examiner states at page 11, first paragraph, of the Final Rejection that:

> The breadth of the claims is quite large. The elected invention is directed to a method of administering any type of cell to an undefined area of a human body to grow new cardiac muscle and a new artery (of any type or location) to achieve growth of a new portion of a pre-existing heart.

Firstly, the claims in issue require cells, stem cells, and bone marrow stem cells. One of ordinary skill in the art appraised of the specification disclosure would readily comprehend the type of cell, i.e., stem cell, required for promoting morphogenesis, e.g., artery growth. Secondly, the claims require growing new cardiac muscle and a new artery which limits the selected placement area to those locations that result in cardiac muscle growth and artery growth in the patient's heart. Regarding the degree of repair, Examples 18 and 19 describe using readily available commercial devices to assess blood flow through the new artery and thus determine the degree of success. There is no requirement that an applicant's claims set forth the practical limits of operation for the invention. One must look to the specification, not the claims, in determining compliance with the first paragraph of the statute. It is clear that the Examiner, in determining compliance with the enablement requirement of the statute, has ignored the scope of enablement provided by the specification as a whole. The Examiner's limited evaluation of Appellant's specification constitutes reversible error. See In re Johnson and Farnham, supra., and In re Fuetterer, 319 F. 2d 259, 265, 138 USPQ 217, 223 (CCPA 1963), cited therein. Moreover, the Examiner's rejection fails to specifically address the inventions of claims 270 and 271 requiring placing cells adjacent dead or damaged portions of the patient's heart and the inventions of claims 272 and 273 requiring injecting stem cells directly into the patient's heart.

As demonstrated earlier, none of the claims in issue require *de novo* formation of an artery; and thus the Examiner has conditioned the enablement rejection on a lack of enablement regarding the unclaimed and undisclosed formation of *de novo* arteries. Being that the Examiner's stated condition has not been met, the rejection must fail.

Except for the unidentified "contradictory state of the prior art" and the failure of the claims to recite "dosages," the factors listed by the Examiner in the above conclusory statement correspond to the Wands factors, which were fully addressed and rebutted earlier. Again, the Examiner has provided no evidence to support her conclusion. Regarding the alleged "contradictory state of the prior art," the Examiner has failed to identify any pre- or post-filing publications presenting evidence in regard to the subject matter of the claims on appeal, which contradicts the objective enablement provided by the instant application. The references cited by the Examiner on page 13 of the Final Rejection to "show the state of the prior art" were specifically directed to the inventions defined in claims 248, 249, and 274-277, which claims are directed to subject matter that is not at issue in the present appeal. The Examiner failed to articulate how such prior art is relevant to establishing a *prima facie* case of lack of enablement of the subject matter called for by the appealed claims *vis-à-vis* the objective enablement provided by the instant specification. To the extent the Examiner is challenging the predictability of Appellant's described cardiac muscle and artery growth, the Perin et al. publication (hereinafter "Perin" and of record), which describes implanting BMC's to provide heart repair suffices to ally such challenge. Perin provides autopsy proof that such heart repair involves both cardiac muscle and artery growth. Regarding "prior art," none has been identified or cited by the Examiner against Appellant's claims and for good reason.

Appellant was the first to disclose and claim a method for treating a human heart by implanting cells, such as stem cells, and growing new cardiac muscle and arteries.

Regarding dosages, it is axiomatic that claims do not have to recite dosage levels where dosage levels would be understood by those skilled in the art. As succinctly stated in MPEP Section 2164.01(c):

> It is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. 112, first paragraph.

Prophetic Examples 18, 19, and 36 describe methods for carrying out the invention including dosage amounts for promoting artery growth and heart repair. Appellant's specification describes new artery growth and heart repair by direct injection of growth factor cells in dosage ranging from approximately 6.25×10^6 (Example 18 & 36) to approximately 12.5×10^6 (Example 19). Available off-the-shelf cDNA clones (nucleic acids) are directly injected into either the cardiac muscle (Example 19) or the coronary artery (Example 36). Each example describes repairing a damaged heart by forming a new artery which results in increased coronary blood flow. Each example also discloses slowly injecting the growth factor to avoid any carry away. Example 18 discloses that a containment system may be used. While these examples employ nucleic acids, one skilled in the art reading the specification, which teaches that cells, i.e., stem cells, possess equivalent activity to genes (nucleic acids) and other genetic material, in forming a new artery and repairing a dead or damaged portion of a heart, would be able to easily extrapolate the number on a weight basis of mononuclear cells required to obtain

equivalent results. Note in this regard that Strauer discloses injecting six (6) to seven (7) times with 1.5 to 4 x 10^6 cells without disclosing any difference in results over the entire dosage range. Therefore, there is no significant clinical difference between Appellant's 6.25 to 12.5 x 10^6 and Strauer's 9 to 28 x 10^6 dosage ranges. Further, such skilled person would understand that intravenous or intraluminal administration routes would generally require larger doses than the direct injection route of Examples 18, 19 and 36, and, for example, simply doubling the dosage to 12.5 to 25 x 10^6 cells would essentially encompass Strauer's entire range.[1] It is clear from Strauer that there is no risk for over-dosing, particularly using autologous BMC's, which are contemplated in Appellant's specification. cf. In re Bundy, 642 F. 2d 430, 434, 209 USPQ 48, 51-52 (CCPA 1981). The Examiner has failed to establish why one skilled in the art would not be able to extrapolate those examples across the entire scope of the claims. See MPEP Section 2164.02.

The limited evaluation of Appellant's specification performed by the Examiner in determining compliance with the enablement requirement of the statute fails to comport with current law and constitutes reversible error. In re Johnson and Farnham, supra. That the Examiner intended to so limit her review of the application disclosure was clearly demonstrated above.

When properly considered, there should be no doubt that the application's disclosure, including the above specifically identified passages, fully enables one skilled

[1] The conversion for dosages of nucleic acids to corresponding dosages of cells was conducted as follows. Examples 19 and 36 specified dosages of 500 micrograms (ug) and 250 ug, respectively. The weight of nucleic acids of an average cell was considered to equal 40 picograms (pg). The described dosages of 250 and 500 ug when converted to pg by multiplying by 10^6 equals 250 x 10^6 pg and 500 x 10^6 pg. Since nucleic acids of an average cell have an average weight of 40 pg, a conversion is made by dividing 250 x 10^6 and 500 x 10^6 by 40 to arrive at the equivalent cell dosages, which are 6.25 x 10^6 and 12.5 x10^6, respectively.

in the medical art to make and use the invention. The Board's attention is once again respectfully directed to Appellant's specification at page 21, lines 4-15, where it is disclosed that growth factors may be administered by a wide variety of techniques, including injection. In addition, the Board's attention is also directed to Appellant's specification at page 45, line 1-16, where it is disclosed that arteries may be grown in a heart by injecting a gene (non-elected species of growth factor) into muscle at a desired site. Moreover, Appellant's specification at page 46, lines 3-7, indicates that seeding with cells and/or genes adjacent a dead cardiac muscle grows new arteries. Seeding is a generic term that includes injection. Example 19 describes repairing a damaged portion of a human patient's heart by slowly injecting (to avoid leakage) a growth factor solution into the patient's cardiac muscle adjacent a clogged artery and growing a new artery and teaches testing for blood flow through the new artery using available commercial devices. Example 36 describes repeating the injection process of Example 18 for growing a new coronary artery, and both examples disclose dosages for obtaining the desired artery growth. That Examples 19 and 36 describe cDNA clones as growth factor species is not important because the specification is replete with disclosure that if cells, such as stem cells and more specifically a patient's own stem cells, are implanted/reimplanted differentiation and morphogenesis into an organ, i.e., artery, occurs. One reasonably skilled in the art appraised of such disclosure would readily be able to predict and comprehend that stem cell growth factors are equivalent to cDNA clones in providing the desired artery formation.

It is a fact that the disclosed administration techniques were well established in the medical art prior to Appellant's invention and must be considered in any evaluation of

enablement. It is also a fact that cells, including stem cells, were well known and characterized prior to Appellant's claimed invention. The Board is respectfully requested to take Official Notice of the fact that processing bone marrow and peripheral blood for recovering mononuclear stem cells was routine in the medical arts prior to Appellant's invention. Typically, bone marrow transplant procedures involved removing bone marrow from the patient which is filtered, treated, and transplanted immediately or frozen and stored for later use. Another established fact—that stem cell banks were created as early as the 1950's–indicates that those skilled in the medical art were familiar with harvesting, handling, culturing, preserving, separating, and storing, etc. such stem cells. The handling and treatment of cells, as well as stem cells, has been long known and practiced in the medical art prior to Appellant's filing date. In this regard, see the Trigg 2002 publication in Pediatric Transplantation entitled, "Milestones in the Development of Pediatric Hematopoietic Stem Cell transplantation – 50 Years of Progress" (of record). As mentioned in this publication, stem cell handling and preparation techniques have been known for decades. The publication provides evidence of the fact that stem cells harvested from bone marrow and from blood of patients has long been known and isolated as part of national blood bank programs. Further, the Board is referred to three publications (all of record); namely: (1) Areman, et al. 1990 publication in Prog. Clin. Biol. Res., entitled, "Automated Isolation of Mononuclear cells using the Fenwal CS3000 blood cell separator;" (2) Angelini, et al. 1990 publication in Haematologica, entitled, "Human bone marrow processing using Cobe 2991 and CS 3000 blood cell separators for further ex vivo manipulation;" and (3) Janssen, et al. 1992 publication in J Hematother, entitled, "Use of the Terumo SteriCell for the processing of bone marrow and peripheral

blood stem cells," which confirm the above-mentioned facts. In addition, the Caplan 1991 publication in Journal of Orthopaedic Research entitled, "Mesenchymal Stem Cells" (of record) reported culturing human bone marrow and isolating mesenchymal stem cells for growing bone in murine models. Appellant believes that such evidence confirms the fact that cells, including stem cells, were well known and characterized prior to Appellant's claimed invention.

Once the relevant materials and administration techniques set forth in Appellant's specification are properly considered in their entirety, Appellant believes that there should be no question that one skilled in the medical art is enabled to make and use the claimed invention. This conclusion is reinforced by the fact that the materials and administration techniques, but not the inventive result, were well known when the instant application was filed.

Appellant submits that the Examiner has apparently failed to comprehend that Appellant has used old and routine administration techniques and old materials to achieve a remarkable new result, which is repair of dead or damaged heart tissue. Inasmuch as the claimed administration techniques and materials were well known to those skilled in the art, a person skilled in the medical art would not require an extensive, detailed description of such old elements of the invention and thus would be enabled to make and use the claimed invention once guided and directed to the administration techniques and materials by Appellant's specification. It is noted that the Examiner has not challenged the fact that these elements were known as of the filing date of the instant application, and for good reason.

In summary, Appellant believes that the Examiner's evidence of lack of enablement, which comprises the Examiner's erroneous assessment of Strauer and Deb, as discussed above, when considered *vis-à-vis* the evidence of enablement provided by Appellant's specification combined with a fair and reasonable reading of Strauer and Deb, coupled with Wollert et al. (hereinafter "Wollert" and of record), fails to establish a *prima facie* case of lack of enablement under current law. Note that Wollert is cited as evidence that the high pressure technique of Strauer is not necessary, and thus the Examiner's contention that the instant disclosure's lack of including the post-filing administration technique of Strauer is nonenabling is patently erroneous. It has been further demonstrated above that the Examiner's conclusion is not supported by sound, objective evidence. Rather, the conclusion is speculative and thereby amounts to no more than the Examiner's opinion. Thus, this rejection should be reversed.

Assuming, *arguendo*, that the Examiner somehow met the burden of establishing a *prima facie* case of lack of enablement, Appellant believes that any such case has been rebutted by the submission of the multiple Declarations of two experts in the field, Dr. Richard Heuser and Dr. Andrew E. Lorincz (all of record). Such Declarations are set forth in the Evidence Appendix (Items 14-22). The conclusions set forth in the respective Declarations establish an objective fact that is highly material to a determination of enablement. These two highly skilled medical experts read relevant portions, including generic and non-elected species portions, and reached the determination that one skilled in the medical arts, armed with the knowledge in the disclosures, would be enabled to practice the claimed method and to predictably anticipate the results defined therein without need for resorting to undue experimentation. See paragraphs 5-7 of the Third

Supplemental Declaration of Dr. Lorincz and paragraphs 5-7 of the Fourth Supplemental Declaration of Dr. Heuser.

The Examiner attempted to diminish the weight to be accorded to such Declarations by essentially rearguing that more than routine experimentation would be required. Moreover, the Examiner's arguments regarding the Declarations do not appear to be directly related to the claims on appeal. Instead, the Examiner's arguments relate to subject matter contained in withdrawn claims. Other than restating her opinion, the Examiner has not met her burden of addressing the probative value of the objective evidence in Appellant's Declarations. By failing to articulate adequate reasons to rebut the Heuser and Lorincz Declarations, the Examiner "failed to consider the totality of the record for the purpose of issuing a final rejection and thus erred as a matter of law." In re Alton, 76 F.3d 1168, 37 USPQ2d 1578 (Fed.Cir. 1996). It is trite law that the Examiner must consider the probative value of such evidence *vis-à-vis* any asserted *prima facie* case. See In re Oetiker, at 1445, 24 USPQ 2d at 1444. In re Keller, 642 F.2d 413, 208 USPQ 871, (CCPA 1981). In the absence of critical analysis, the Examiner appears to be relying solely upon her opinion rather than assessing weight to the objective evidence proffered in the Declarations. The Examiner, not being a skilled person in the medical art, must give weight to these expert opinions rather than substitute her own opinion. See In re Neave, 370 F.2d 961, 152 USPQ 274, (CCPA 1967).

In the Final Rejection, the Examiner has questioned the presence or absence of factual support for the expert opinions. In doing so, the Examiner has erroneously implied that the experts relied upon "some publications" in addition to Appellant's disclosure in reaching their opinions. A concise reading of the Declarations reveals that

the experts relied solely upon the guidance and direction in the application's generic and specific disclosures pertaining to the claims coupled with their skills in the medical art in rendering their conclusions. Appellant, likewise, relies upon such disclosure.

As a final point, the Board's attention is again respectfully directed to the In re Wands decision, which led to the grant of a patent. The Court found that the Patent and Trademark Office's determination of nonenablement was unsupported by the evidence in the record. The Court further noted that the skill level in the art was high and that known materials were utilized in the practice of the invention in weighing the evidence. The instant fact situation is similar to that of In re Wands because the skill level is also high and known administration techniques and known materials are also utilized in the practice of the invention. In addition to such factual parallelism, Appellant provided expert objective evidence in the form of the Declarations of Drs. Heuser and Lorincz. These medical experts read portions of the specification setting forth the generic invention and elected and non-elected species of such generic invention and determined that one skilled in the medical arts, armed with the guidance and direction in the specification disclosures, would be enabled to practice the methods defined in the claims on appeal and to predictably anticipate the results defined therein without need for resorting to undue experimentation. When the guidance and direction provided by Appellant's specification disclosure, the level of knowledge and the content of the prior at the time of the invention as established in the record and Appellant's declaration evidence are interpreted in a reasonable manner, analysis considering the factors in In re Wands compels a conclusion that undue experimentation would not be required to practice the invention called for in the appealed claims.

CONCLUSION AND RELIEF SOUGHT

In view of the foregoing, Appellant urges the Board to reverse the outstanding rejection of claims 236, 238, 239, 243, 244, 246, 247, 250, 251, 253, 257-263, 268-271, and 280-285 under 35 U.S.C. §112, first paragraph, and respectfully requests that the instant application be passed to issue.

Respectfully submitted,

Dated: Feb. 20, 2007

Gerald K. White
Reg. No. 26,611
Attorney for Appellant

Dated: Feb. 20, 2007

Charles N. Lovell
Reg. No. 38,012
Attorney for Appellant

GERALD K. WHITE & ASSOCIATES, P.C.
205 W. Randolph Street
Suite 835
Chicago, IL 60606
Phone: (312) 920-0588
Fax: (312) 920-0580
Email: gkwpatlaw@aol.com

CLAIMS APPENDIX

Claims 236, 238, 239, 243, 244, 246, 247, 250, 251, 253, 257-263, 268-271, and 280-285 are pending in the application, are under final rejection, are being appealed, and are listed below.

Claim 236 A method of growing a new portion of a pre-existing heart comprising the steps of placing a growth factor in a body of a human patient and growing new cardiac muscle and growing a new artery in said heart.

Claim 238 The method of claim 236, further comprising repairing a dead portion of said heart.

Claim 239 The method of claim 236, further comprising repairing a damaged portion of said heart.

Claim 243 The method of claim 236, wherein said growth factor comprises a member selected from the group consisting of cells, cellular products, and derivatives of cellular products.

Claim 244 The method of claim 243, wherein said growth factor comprises a cell.

Claim 246 The method of claim 245, wherein said cell comprises a stem cell.

Claim 247 The method of claim 236, wherein said growth factor is placed in said patient by injection.

Claim 250 The method of claim 247, wherein said injection is intramuscular.

Claim 251 The method of claim 236, wherein said growth factor is placed in said patient by a carrier.

Claim 253 The method of claim 236, wherein said growth factor comprises a gene and a cell.

Claim 257 The method of claim 236, wherein said growth factor is locally placed in said body.

Claim 258 The method of claim 238, wherein said growth factor is locally placed in said body.

Claim 259 The method of claim 239, wherein said growth factor is locally placed in said body.

Claim 260 The method of claim 243, wherein said growth factor is locally placed in said body.

Claim 261 The method of claim 236, wherein said growth factor comprises living stem cells harvested from bone marrow.

Claim 262 The method of claim 238, wherein said growth factor comprises living stem cells harvested from bone marrow.

Claim 263 The method of claim 239, wherein said growth factor comprises living stem cells harvested from bone marrow.

Claim 268 The method of claim 262, wherein said stem cell is placed in said patient by injection.

Claim 269 The method of claim 263, wherein said stem cell is placed in said patient by injection.

Claim 270 The method of claim 258, wherein said growth factor comprises a cell and said cell is placed adjacent to said dead portion of said heart.

Claim 271 The method of claim 259, wherein said growth factor comprises a cell and said cell is placed adjacent to said damaged portion of said heart.

Claim 280 The method of claim 236 further comprising calculating blood flow through said newly grown artery.

Claim 281 The method of claim 238 further comprising calculating blood flow through said newly grown artery.

Claim 282 The method of claim 239 further comprising calculating blood flow through said newly grown artery.

Claim 283 The method of claim 236 further comprising observing said newly grown artery.

Claim 284 The method of claim 238 further comprising observing said newly grown artery.

Claim 285 The method of claim 239 further comprising observing said newly grown artery.

EVIDENCE APPENDIX

1. Office Action dated February 22, 2006 (page 6, lines 1-8) in co-pending application Serial No. 09/794,456 filed February 27, 2001.

2. Strauer et al. publication in Circulation entitled, "Repair of Infarcted Myocardium by Autologous Intracoronary Mononuclear Bone Marrow Cell Transplanattion in Humans" cited by Applicant as Exhibit E in Declaration of Dr. Richard Heuser filed June 17, 2003 (in connection with concurrently-filed Amendment).

3. Deb et al. publication in Circulation entitled, "Bone Marrow-Derived Cardiomyocytes Are Present in Adult Human Heart" cited by Applicant as Exhibit II in the Amendment filed February 17, 2004.

4. Murry et al. 1996 publication in J. Clin. Invest. entitled, "Skeletal Myoblast Transplantation for Repair of Myocardial Necrosis" cited by the Examiner in the November 28, 2003 Office Action.

5. Nabel et al. U.S. Patent No. 5,328,470 cited by the Examiner in the November 28, 2003 Office Action.

6. Strauer et al. 2005 publication in Circulation entitled, "Regeneration of Human Infarcted Heart Muscle by Intracoronary Autologous Bone Marrow Cell Transplantation in Chronic Coronary Artery Disease" cited by Applicant as Exhibit D in the Amendment filed November 21, 2005.

7. Perin et al. 2005 publication in Circulation entitled, "Transendocardial, Autologous Bone Marrow Mononuclear Cell Injection in Ischemic Heart Failure" cited by Applicant as Exhibit E in the Amendment filed November 21, 2005.

8. Trigg 2002 publication in Pediatric Transplantation entitled, "Milestones in the Development of Pediatric Hematopoietic Stem Cell transplantation – 50 Years of Progress" cited by Appellant as Reference AO in the 3rd Supplemental Information Disclosure Statement filed July 30, 2004.

9. Areman et al. 1990 publication in Prog. Clin. Biol. Res., entitled "Automated Isolation of Mononuclear cells using the Fenwal CS3000 blood cell separator" (as found on the website www.ncbi.nlm.nih.gov) cited by Appellant as Exhibit F to Appellant's Appeal Brief filed June 13, 2005.

10. Angelini et al. 1990 publication in Haematologica, entitled, "Human bone marrow processing using Cobe 2991 and CS 3000 blood cell separators for further ex vivo manipulation" (as found on the websitewww.ncbi.nlm.nih.gov) cited by Appellant as Exhibit G to Appellant's Appeal Brief filed June 13, 2005.

11. Janssen et al. 1992 publication in J Hematother, entitled, "Use of the Terumo SteriCell for the processing of bone marrow and peripheral blood stem cells" (as found on the website www.ncbi.nlm.nih.gov) cited by Appellant as Exhibit H to Appellant's Appeal Brief filed June 13, 2005.

12. Caplan 1991 publication in Journal of Orthopaedic Research, entitled, "Mesenchymal Stem Cells" cited by Applicant as Exhibit E in the Amendment filed June 26, 2006.

13. Wollert 2004 publication in The Lancet entitled, "Intracoronary autologous bone-marrow cell transfer after myocardial infarction: the BOOST randomized controlled clinical trial" cited by Applicant as Reference AP in the 3rd Supplemental Information Disclosure Statement filed July 30, 2004.

14. Declaration of Dr. Richard Heuser filed on June 17, 2003.

15. Supplemental Declaration of Dr. Heuser filed on February 17, 2004.

16. 2nd Supplemental Declaration of Dr. Heuser filed on dated July 30, 2004.

17. 3rd Supplemental Declaration of Dr. Heuser cited by Appellant as Exhibit I in the Appeal Brief filed June 13, 2005.

18. 4th Supplemental Declaration of Dr. Heuser cited by Applicant as Exhibit A in the Amendment dated June 26, 2006.

19. Declaration of Dr. Andrew E. Lorincz filed on June 17, 2003.

20. Supplemental Declaration of Dr. Andrew E. Lorincz filed on February 17, 2004.

21. 2nd Supplemental Declaration of Dr. Andrew E. Lorincz filed on July 30, 2004.

22. 3rd Supplemental Declaration of Dr. Andrew E. Lorincz cited by Applicant as Exhibit B in the Amendment dated June 26, 2006.

RELATED PROCEEDINGS APPENDIX

1. Appeal related to Serial No. 09/794,456, filed February 27, 2001, Appellant's Brief filed February 8, 2007.